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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,583	DOSHI, RAJIV	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) *21-23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/04;10/03;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending.

Information Disclosure Statement

1. The information disclosure statement filed July 8, 2004, July 22, 2004 and October 2, 2003 have been considered.

Claim Objections

2. Claims 21-23 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from other claims in the alternative and not simultaneously; claims 21-23 depend from both claim 1 and 17 simultaneously which is improper form. See MPEP § 608.01(n). Accordingly, the claims 21-23 have not been further treated on the merits.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-3,5,10,13-14, 16, 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Aoki et al (PG-Pub 2001/0041181 A1, filing date June 15, 2001).

3. **Instant claims 1, 2, 3 and 5:** Aoki et al disclose the instantly claimed invention directed to a method of treating a urologic disorder, the method comprising the step of:

4. Intravesically (locally [0022] administering a neurotoxin for treating urinary, gall bladder (a type of bladder disorder) and rectum smooth muscle disorder[0014]) administering a neurotoxin [0017,0020-0021] a to the host [0027, human] in an effective amount [see [0026-0028] to treat the urologic disorder [urinary smooth muscle disorder; gall bladder, 0014].

5. **Instant claim 10**: administering to said host at least one additional agent to treat said urologic condition (see [0023, 0028 "DYSPORT' (a combination of neurotoxins]), also [0031 "anesthesia"]).

6. **Instant claim: 13-14,16**: means for delivering the neurotoxin include a delivery device that comprises a reservoir (needle) associated with a electromotive, mechanical device ([0031 "fine, hollow, Teflon-coated needles, guided by electromyography"]).

7. The disclosed methods are carried out with the pharmaceutical compositions disclosed, the compositions comprising:

8. **Instant claims 17-19**: An effective amount of one or more neurotoxins (see [0028, 0027] and an intravesical delivery vehicle ([0022-0023: albumin, solution, sodium chloride, glycerol, sugars] together with a delivery device [0031, fine hollow, Teflon coated needle, guided by electomyography] . The reference anticipates the instantly claimed invention.

9. Claims 1-2,5-10,13,15 are rejected under 35 U.S.C. 102(e) as being anticipated by Naumann (US Pat. 6,776,991, effective filing date June 26, 2002).

10. **Instant claims 1, 2, 5, 13,15**: Naumann disclose the instantly claimed invention directed to a method of treating a urologic disorder, the method comprising the step of: Intravesically ("insertion of a controlled release implant" see col. 11, lines 35-36, locally to a penis, col. 10, lines 11-17) administering a neurotoxin (botulinum toxin, see abstract; col. 9, lines 40-67, especially, line 47, 50-53 and 62-67) to the host (human or non-human animal, see col. 9, lines 60-61) in an effective amount (col. 10, lines 1-10) to treat the urologic disorder (priapism, see col. 1, lines 5-8). The polymeric composition being a controlled release implant composition, a type of reservoir that functions as delivery vehicle.

11. **Instant claim 6-9**: is administered with at least one neurotoxin permeability modulating agent, wherein Naumann discloses the combination of the neurotoxin together with "non-neurotoxin compounds can be administered prior to, concurrently with or subsequent to administration of the neurotoxin" which evidence a proved adjunct effect such as enhanced or a more rapid onset of denervation" and therefore serve as a permeability modulating agent for the botulinum toxin to exert its therapeutic effect" see col. 14, lines 41-46.

Instant claim 10: administering to said host at least one additional agent to treat said urologic condition (see col. 14, lines 32-33 and 37-39 "two or more neurotoxins"; "a combination of any two or more of the botulinum serotypes A-G").

The disclosed methods are carried out with the pharmaceutical compositions disclosed, the compositions comprising:

Instant claims 17-19: An effective amount of one or more neurotoxins (see col. 4, lines 30-45) and an intravesical delivery vehicle and device that comprises the neurotoxin together with the delivery vehicle ("non-neurotoxin compounds can be administered to enhance or cause the more rapid onset of denervation" (see col. 14, lines 41-45)). The neurotoxin is botulinum toxin (col. 11, lines 61-67), the delivery vehicle is the non-neurotoxin compounds which enhance or cause the more rapid onset of denervation and the device loaded with both of these compounds is the controlled release implant for treating a urogenic disorder.

12. Claims 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO99/03483 (University Technology Corporation).

13. (Instant claims 17-18) WO99/03483 disclose pharmaceutical compositions for treatment of urologic and related disorders (see title), the compositions comprising a neurotoxin (see title, abstract) in an effective amount ("provide dosages and methods of administration for compositions useful for the prevention and treatment of neurological-urological conditions", see page 5, lines 14-17)) for treating a urologic disorder, the composition being one that serves as an intravesical delivery vehicle, wherein the neurotoxin may be botulinum toxin A (see page 5, line 28), capsaicin, resinoferatoxin or alpha-bungotoxin (see page 6, lines 1-2). The pharmaceutical compositions are in the form of a liquid, powder, cream, emulsion, pill, troches, suppositories, suspension or solutions (see page 7, lines 19-23). These forms are forms that serve as an intravesical delivery vehicle, specifically the liquid carrier vehicle, emulsion carrier vehicle, the cream carrier, vehicle suppository formulation vehicle, solution carrier vehicle. The reference anticipates the instantly claimed invention.

14. Claims 17-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Deem et al (US PG-Pub 2004/0226556 A1, effective filing date May 13, 2003).

Deem et al disclose the instantly claimed pharmaceutical preparation that comprises:

15. **Instant claim 20**: a catheter (see paragraph [0036] and [0018]).

16. **Instant claim 19**: that is loaded with a pharmaceutical preparation (see "in fluid communication with a source of liquid neurotoxin [0021]" "for application to a target treatment area" [0016 in a delivery vehicle ([0018, neurotoxin application assembly, "a needle-less injection assembly", in a liquid [0019].

17. **Instant claim 18**: the neurotoxin is botulinum toxin (see [0006 "Botox" "botulinum toxin serotype A"]

18. **Instant claim 17**: preparation of a neurotoxin in an effective amount [the preparation being an effective amount of a neurotoxin ("controlled and direct application of the neurotoxin to the desired tissue for safe and effective therapy [0008]), and is filled with neurotoxin in liquid form [0035].

19. in an intravesical delivery vehicle (any vehicle that can deliver the preparation to the bladder muscles that comprises a catheter). While the catheter assembly of Deem et al is discussed with respect to bronchial applications, the catheter is formulated to deliver the neurotoxin to the desired tissue [see 0008]) and comprises either a needleless delivery vehicle (needleless injection vehicle) or a nebulizer assembly [see 0018], in a liquid [0020 and 0022].

20. Deem et al anticipate the instantly claimed compositions that comprise the same or equivalent components, the recited intended use not defining over the applied prior art.

21. Claims 1,3,4,11 are rejected under 35 U.S.C. 102(b) as being anticipated by McCabe et al (US Pat. 6,172,041).

McCabe et al disclose the instantly claimed invention directed to a method of treating a urologic disorder, wherein the disorder is urinary incontinence, the method comprising the step of:

Instant claim 1,3 and 4: Administering a neurotoxin (conotoxin) to a host (mammal) in an amount to treat urinary incontinence (see Example 18 col. 33-34: In Vivo Activity of Conantokin G in Animal Model of Urinary Incontinence , Female Wistar rats are anesthetized with urethane and, following tracheotomy (for ventilation after skeletal muscle paralysis) and jugular and carotid cannulation (for drug delivery and blood pressure recording, respectively), laminectomies are performed at C7-T2 and T11-S1 through a midline dorsal incision. The back is temporarily closed and the animal is placed abdomen up. A midline incision is made from the sternum to the pubis. The ureters are isolated, ligated and cut proximally, and saline soaked gauze wicks are positioned at the cut end to exit the abdominal incision for urine elimination. Conantokins are introduced intrathecally and changes in blood and bladder pressure responses under constant drive are monitored, recorded and taped. Control studies are made with hexarnethonium bromide and all studies finish with hexamethonium bromide administration.

Instant claim 11: Administration of the neurotoxin (conotoxin) was accomplished utilizing a double lumen urethral catheter passed through a cystotomy at the dome of the bladder and seated in the urethral opening at the level of the internal sphincter. A second, single lumen catheter is positioned, through its own cystotomy, into the bladder. Both catheters are tied in with suture, and connected to pressure recording transducers and filling/perfusion syringes via three-way stopcocks. Conatokin G was administered and the 30 nmol dose eliminated all lower urinary tract activity. Similar effects were seen for conantokin T. Further effects of Con G and Con T on bladder contraction amplitude and on EUS EM G activity are shown in FIGS. 17 and 18. The conantokins appear to be more discriminatory in their inhibitory effect on striated sphincter than on bladder, compared to other NMDA antagonists. Thus, it is possible to dose the conantokins in such a manner to selectively decrease bladder/sphincter dyssynergia in spinal cord-injured patients.

The reference anticipates the instantly claimed invention.

Claim Rejections - 35 USC § 103

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over McCabe et al as applied to claims 1 3,4,11 above, in view of Gillies.

See discussion of McCabe et al above. McCabe et al administered a neurotoxin (conotoxin) to the bladder of a host (see col. 34, lines 56-32) to treat incontinence utilizing a double lumen catheter (see col. 33, lines 33) together with a single lumen catheter (see col. 33, line 36), but differs from the instantly claimed invention by failing to show the administration step being carried out with a catheter with an inflatable component.

Gillies teaches a catheter with an inflatable component for the administration of a neurotoxin in an analogous art for the purpose of selectively delivering (abstract) a neurotoxin to a host within a wide range of medical procedures (see col. 23, lines 46-47 and 62) , wherein said delivering is carried out in "real time or near real time" which permits the observation and assessment of the patient's response to the delivered drug present in the tissue (see col. 1, lines 18-19).

It would have been prima facea obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of McCabe et al that utilizes both double and

single lumen catheters in a method of delivering a neurotoxin to a host with the inflatable catheter of Gilles that delivers a neurotoxin to a host because both references are directed to the administration of a neurotoxin to a host patient for the purpose of treating a condition or disorder and Gilles teaches the advantage provided by an inflatable catheter to be the selective administration of the desired neurotoxin to tissue for assessment of the patients response to the drug in real time or near real time.

In the absence of a showing of unexpected results, McCabe et al in view of Gilles obviates the instantly claimed invention because the person of ordinary skill in the would have been motivated by the reasonable expectation of success of substituting the inflatable catheter of Gilles et al for the mode of administration of McCabe et al because Gilles et al teaches the inflatable component containing catheter successfully defines means for selective delivery of a neurotoxin in a method of treating a patient disorder.

Conclusion

24. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
25. US Pat. 5,085650 is cited to show suppositories for bladder application .
26. Sanders et al (US Pat. 5,766,605 is cited to show a suppository for treatment of spastic colitis.
27. Schmidt (US Pat. 6,667,041 and 6,365,164) are cited to show a method and pharmaceutical compositions that comprise a neurotoxin for therapy of urologic disorders (see title).
28. Donovan et al (US Pat. 6,383,509 and 6,312,708) are cited to show controlled release neurotoxin containing pharmaceutical preparations incorporated by reference by Naumann above.
29. PG-PUB 20030185860 is cited to show a balloon catheter and stent coated with botulinum toxin [0134, 0138, 0140, 0143].
30. Borodic, GE (US Pat. 5,401,243) is cited to show Dykstra et al in US Pat. 4,932,936 to suggest the administration of botulinum toxin in the treatment of spasmodic sphincter muscle which leads to urinary incontinence (neurogenic bladder).

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
March 9, 2005

L. F. Smith

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